AMENDMENTS

IN THE SPECIFICATION:

Under 37 C.F.R. § 1.121(b), please amend the paragraph beginning on page 9, line 5, as follows:

Although the D_1 agonists for use in the present invention possess properties as full D_1 dopamine receptor agonists, for some patients, the agonist chosen should also have some D_2 agonist properties. Exemplary in Parkinson's disease, the degree and nature of the D_2 properties should be individualized to maximize the therapeutic benefit to the patients, based on the relative amount of dyskinesias, emesis, and/or mental disturbance caused by prior use of levodopa and/or apomorphine. Thus, patients who have demonstrated large dyskinetic or emetic responses to levodopa or apomorphine should be given full D_1 agonists with greater D_1:D_2 selectively, or full D_1 agonists in which the D_2 properties have a high degree of functional selectively. Dihydrexidine, dinapsoline, and ~~dioxyline~~ dinoxyline all exhibit some D_2 agonist properties. Dihydrexidine is ten-fold D_1:D_2 selective, dinapsoline is five-fold D_1:D_2 selective, and dinoxyline has equally high affinity for both types of receptors.

Please amend the paragraph beginning on page 33, line 24, as follows:

Surgery. Rats were pretreated with 25 mg/kg desipramine (s.c.) approximately 30 minutes before surgery. Rats were anesthetized by inhalation of isoflurane (1.5 to 4.0%) and placed in a stereotaxic apparatus. An infusion cannula was placed in the medial forebrain bundle at the coordinates A.P. -3.8 mm, M.L. -1.5 mm, and D.V. -3.8 mm relative to bregma according to the atlas of Paxinos and Watson (1986). Ten micrograms of 6-OHDA (6-hydroxydopamine; Sigma Chemical Co., St. Louis, MO) ~~in a volume of 4 il~~ in a volume of 4 µL was infused ~~at a rate of 0.5 il/min~~ at a rate of 0.5 µL/min in a vehicle of 0.01% ascorbate. After a 14-day recovery period, rats were prescreened for rotation in response to *d*-amphetamine (5 mg/kg) and to apomorphine (0.3 mg/kg) 1 week later. Animals that responded to both *d*-amphetamine (>800 rotations in 3 h) and apomorphine (>100 rotations in 1 h) were retained for further study.

Please amend the paragraph beginning on page 34, line 3, as follows:

Testing of compounds began on day 28 postsurgery in each case. A new group of 6-OHDA-lesioned rats was used for each new study. In some studies, rats were implanted with a subcutaneous 14-day osmotic minipump (model 2 ML2, Alza, Palo Alto, CA) with ~~a flow rate of 5.0 il/h~~ a flow rate of 5.0 µL/h. The rats were re-anesthetized with

1.5 to 4% isoflurane, a small incision was made on the back of the neck, and the minipump was placed subcutaneously in the cavity. The incision was closed with sterile wound clips. Before implantation, minipumps were incubated in sterile saline (37 °C) to ensure outflow at the time of implantation. The minipumps were used to administer dinapsoline, or vehicle (50% dimethyl sulfoxide (DMSO), 12.5% ascorbic acid).

Please amend the paragraph beginning on page 34, line 14, as follows:

Striatal Dopamine Content. In a subset of animals, striatal dopamine content was measured to confirm the extent of the 6-OHDA lesion. At the completion of the study, animals were anesthetized deeply by CO_2 inhalation and rapidly decapitated using a guillotine. Brains were removed quickly, and kept on ice while right and left striata were isolated, removed, and weighed in individual nonfilter micro-centrifuge tubes containing 0.5 ml of a homogenizing buffer (0.22 N perchloric acid, 0.5% EDTA, 0.15% sodium metabisulfite). The samples were homogenized by sonication for 10 seconds and then centrifuged at 14,000g for 20 minutes. The supernatant was transferred to microcentrifuge tubes with ~~a filter (0.2 im)~~ a filter (0.2 µm) and centrifuged at 14,000g for 2 minutes. The samples were frozen at -80 °C to await HPLC analysis.

Please amend the paragraph beginning on page 34, line 26, as follows:

HPLC Analysis. Thawed samples were analyzed for dopamine content using established high performance liquid chromatography (HPLC)-electrochemical detection methods. Briefly, ~~50 il samples~~ 50 µl samples were injected into the sample loop of an HPLC system using an acetate buffer mobile phase (17% methanol) pumped at 0.4 ml/min. Peaks were separated with a C-18 reverse phase column (3-mm diameter, MD-180, ESA, Chelmsford MA) and detected with a dual coulometric cell (5014B, ESA) and detector (Coulochem II, ESA). Dopamine was analyzed by sequential reduction (-100 mV) and oxidation (350 mV) and was quantified at the latter electrode. Dopamine concentration in each sample was calculated in reference to established standard curves and was represented as picomoles per milligram of striatal tissue. Depletion was calculated as the percentage of dopamine content on the lesioned side relative to the nonlesioned side.